Stroke in Women

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Stroke is the leading cause of disability and is the third leading cause of death in women in the United States. Of the 500,000 patients affected by a new stroke, nearly 200,000 will affect women.[1] In addition, approximately 90,000 American women die each year from a stroke, accounting for 60% of all stroke deaths.[1] The mortality rate from stroke is higher in women; the death rate from stroke is 16%, while it is 8% in men.[2] The reason for the higher death rate is the older age of women at the time of their initial stroke. The impact of stroke in women extends beyond the individual, since women are often the primary care giver to children and are often responsible for the care of an aged or ill spouse.

There are various risk factors that have been identified for stroke; however, except for some unique situations such as pregnancy and the use of oral contraceptives, the risk factors for stroke appear to be the same for men and women. In the last few decades, there has been a decline in the mortality rate from stroke, primarily because of better control of risk factors such as hypertension. However, the rate of the decline has slowed both in men and women.

Hypertension is the leading risk factor for stroke in both men and women. The prevalence of hypertension as a risk factor is two times higher in Afro-American women as compared to Caucasian women.[3] Treatment of hypertension, including isolated systolic elevations, effectively reduces the risk of stroke.[4]

Cigarette smoking is another treatable risk factor for stroke—smoking is a major risk factor for the development of carotid atherosclerosis. Women cigarette smokers have a three-fold increase in the risk of stroke compared to nonsmokers. The risk of stroke increases with the number of cigarettes smoked.[5] The risk of stroke can be reduced by smoking cessation.[5]

After hypertension, heart disease is the most important risk factor for stroke. Cardiac disease accounts for approximately 20% of strokes. Atrial fibrillation is more common in men in all age groups[6]; however, after age 80, the incidence in women approaches that of men.[6] The Stroke Prevention in Atrial Fibrillation (SPAF) study has suggested that in patients less than 75 years of age with no risk factors of congestive heart failure, hypertension or prior thromboembolism aspirin can be recommended.[7] Those less than 75 years with risk factors should be treated with long-term, low-dose warfarin therapy. Patients over age 75 years present a dilemma because the protection is not great with either aspirin or warfarin. The SPAF III study is in progress to further study this question.

Mitral valve prolapse is twice as common in women as in men[8]; however, women do not seem to be more prone than men to have a stroke with this condition.[9]

Oral contraceptives with a higher dose of estrogen have been associated with a 9-times greater incidence of stroke.[10] Women who are over age 35 and are hypertensive or are smokers have the greatest risk of having complications. The lower-dose estrogen preparations effect a lower risk of stroke.[11] Postmenopausal use of conjugated estrogens appears to reduce the risk of vascular disease.[12]

Pregnancy increases the risk of stroke by 3 to 13 times.[13] Some potential etiologies include hypertension, cardiac lesions, including peripartal cardiomyopathy, diabetes, hypercoagulability, or amniotic, fat or air emboli.

Fibromuscular dysplasia (FMD), an uncommon non-atherosclerotic vasculopathy, is more common in women. In one series, 95% of the persons affected with FMD were women.[14]

Therapy for stroke prevention includes aspirin, ticlopidine, or warfarin. Risk factor modification of the treatable causes of stroke is important. In stroke in women, special attention often needs to be paid to assessing the support systems for care of children, a dependent spouse, and for household responsibilities.

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total body water, extracellular fluid volume, total exchangeable body sodium, or plasma volume.[6] Diuretics are widely used, however, they might be most helpful in the subgroup of women with premenstrual weight gain.

When dysphoria, irritability, and other psychological symptoms predominate, a trial of a psychotropic may be helpful. Antidepressants that inhibit serotonin (5HT) re-uptake, such as fluoxetine and clomipramine, have been found to be effective in double-blind trials.[19-21] Other antidepressants have been tried with good results in open trials. Buspirone, a 5-HT1A partial agonist, also has been shown to be significantly more effective than a placebo for irritability, fatigue, pain and social functioning in 34 patients treated with a mean daily dose of 25 mg 12 days prior to menstruation.[22] Alprazolam, a high potency benzodiazepine, given only during the premenstruum also is effective for mood symptoms and global improvement as compared to placebo.[23,24] Longitudinal intermittent treatment studies with this drug are currently in progress. Other psychotropics that have been tried with less promising results include lithium, fenfluramine, naltrexone, and clonidine.

For severe symptoms that do not respond to less invasive treatments, the next step would be to eliminate the ovarian trigger. This can be done through hormonal treatment or through surgical approaches.

Oral contraceptives can suppress ovulation but hormonal cyclicity remains. This probably accounts for the unpredictable response to such agents. Furthermore, some patients develop side effects to oral contraceptives that are similar to symptoms of PMS.[25]

Danazol is a synthetic androgenic derivative of ethisterone which causes hypothalamic pituitary-gonadotrophin suppression. When given continuously in doses that suppress ovulation and menstruation, the symptoms of PMS are abolished.[26,27] Its usefulness is limited because of its androgenic properties in women of childbearing age.

GNRH agonist analogues act by creating a reversible pseudohypophysectomy and, therefore, a pseudomenopause. Depot goserelin, for instance, has been shown to eradicate premenstrual symptoms.[28] Long-term treatment, however, is not feasible because of risks of osteoporosis and atherosclerotic heart disease. Studies are being conducted in combination with adjuvant conventional hormone replacement therapy.

Surgery may be a last resort for severely affected patients unresponsive to other strategies. Total hysterectomy with bilateral salpingo-oophorectomy can eliminate the symptoms of PMS.[29]

Although the etiology of PMS remains unclear there are strategies a clinician can utilize to alleviate symptoms. The problem is an important one and deserves our continued clinical attention and study.

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